REMARKS

The present response is being submitted in reply to the Office action dated July 2, 2003. Claims 15-25 are pending in the application. According to the Office action, claims 15-25 are presently rejected. By the present correspondence, claims 15, 17, 23 and 25 have been amended and claims 16, 18 and 24 have been deleted, the subject matter from the deleted claims being incorporated into the independent claims from which each respectively depends. Reconsideration is respectfully requested in light of the amendments being made hereby and of the following remarks.

Objection to the Specification

The Examiner has objected to the specification for not having included a brief description of the drawings section. Applicant refers the Examiner above where the applicant has amended the specification accordingly. It is respectfully requested that this objection be withdrawn.

Objection of claims 15-25 under 35 U.S.C. 112, second paragraph

Claims 15-25 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Specifically, claims 15 and 17 recite a transdermal therapeutic patch containing three polymer layers, each having a glass transition temperature. Applicant has amended claims 15, 17, 23 and 25 to more clearly define the glass transition temperatures of the three layers by referring to the glass transition temperature of the third layer as "T_g3" in order to differentiate it from that of the first layer ("T_g1"). As such, applicant respectfully requests that this objection be withdrawn.

Rejection of claims 15-25 under 35 U.S.C. 103(a)

Claims 15-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,151,271 (Otsuka et al.) by itself or in view of U.S. Patent No. 6,416,858 (Ercillo et al.). According to the Examiner, Otsuka teaches a pressure sensitive adhering composite medicinal preparation comprising at least two layers, namely at least one macromolecular layer and a polymer layer. The polymer layer contains a polymer or copolymer that has a glass transition temperature of not lower than –50 degrees Celsius, preferably –45 to 75 degrees Celsius. Furthermore, the Examiner states that Otsuka teaches a release liner. The Examiner lastly states that although Otsuka teaches more than three polymer layers, the reference does not exemplify the third layer or a protective layer.

According to the Examiner, Ercillo teaches a multi-layer pressure sensitive adhesive construction containing a facestock (protective layer), a first adhesive layer having a glass transition temperature, the second layer having a glass transition temperature 10 to 50 degrees lower than the first layer, and a release liner. The Examiner also states that Ercillo teaches that the degree of tack possessed by a particular adhesive layer is largely dependent on the glass transition temperature of the layer. As the Examiner explains, if the glass transition temperature is too high, the composition fails to act as an adhesive. If it is too low, then the adhesive composition will flow too readily, which diminishes converting performance.

It is the Examiner's belief that it would have been obvious to one skilled in the art to follow the guidance of Otsuka and incorporate a third layer since Otsuka teaches that the composition should contain at least two layers. The Examiner also states that it would have

been obvious to one of ordinary skill in the art to combine the teachings of Otsuka and Ercillo and manipulate the arrangement of the polymer layers according to the glass transition temperature of the polymer. According to the Examiner, one would be motivated to do so since Ercillo teaches that the manipulation of the adhesive layers based on the glass transition temperature yields the desired converting performance and adherence properties.

As will be explained in further detail below, the applicant respectfully disagrees with the Examiner's conclusions. In support of the applicant's arguments, claims 15, 17, 23 and 25 have been amended to more clearly distinguish the claimed invention from the cited prior art references. Specifically, the claims have been amended to define the presence of an active substance in at least one of the three layers, support for which can be found in claims 16, 18 and 24, which are now deleted.

Applicant respectfully submits that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitation. Applicant respectfully submits that one skilled in the art would have no suggestion or motivation to combine the aforementioned references in order to arrive at the present invention. Additionally, even if one skilled in the art were to consider Otsuka alone, or in combination with Ercillo, each and every limitation of the present invention would not be disclosed, nor would there be a reasonable expectation of success.

Turning first to Otsuka, as the Examiner has already pointed out on page 4 of the

Office action, the reference fails to specifically teach a transdermal therapeutic patch having a third layer. Moreover, nowhere in Otsuka is an active substance release rate-controlling layer (such as that recited in claim 25 of the present application) taught or disclosed.

Applicant also submits that Otsuka does not unambiguously teach that the polymers in the two layers should have different glass transition temperatures. The glass transition temperature of the polymer layer in Otsuka (which corresponds to the second layer of the present invention) should be not lower than –50 degrees Celsius (col. 2, line 24), but preferably should be between –45 degrees Celsius and +75 degrees Celsius (col. 2, line 25). Otsuka also teaches that the macromolecular substance in the adhesive layer (which corresponds to the first or third layer of the present invention) should have a T_g between –70 degrees Celsius and -10 degrees Celsius (col. 3, lines 11-13). Accordingly, there is an overlapping range between –45 degrees Celsius and -10 degrees Celsius, from which it follows that the glass transition temperatures in the two layers may be identical. In other words, the T_g of these two layers in Otsuka may be the same whereas the respective T_g's of the corresponding layers in the present invention are not the same (claims 15, 17, 23 and 25).

As mentioned above, to establish a 35 U.S.C 103(a) *prima facie* case of obviousness, there must be some motivation or suggestion in the references to combine the reference teachings. It is apparent that neither reference contains any suggestion or motivation to combine the references, but rather each suggests a system that teaches away from the present invention.

Applicant further submits that the problem which the Otsuka invention seeks to address is different from the problem which the present invention addresses. According to

Otsuka, the main objective is to prevent drug crystallization in the macromolecular (adhesive) layer and to increase percutaneous drug absorption (col. 1, "Summary of the Invention"). This goal is achieved by providing an additional polymer layer into which the drug substance or auxiliary substance can migrate or diffuse. The polymer layer is produced without adding an active substance and is laminated onto the active substance-containing macromolecular layer, after which the active substance is allowed to migrate into the polymer layer (Example 1, col. 7). Applicant submits that the degree of migration/diffusion of the active substance into and within the polymer layer is mainly affected by the polymer composition (col. 2, lines 28-54) and the glass transition temperature, which should not be lower than –50 degrees Celsius in order to ensure a sufficient degree of migration (col. 2, lines 56-59). For the macromolecular substance layer, which forms the skin-adhesive layer, the reference recommends using substances having a glass transition temperature in the range of –70 degrees Celsius to -10 degrees Celsius to ensure good adhesive properties (col. 3, lines 11-21).

In contrast to the present application described at page 5, second and third paragraphs, Otsuka does not address the problem of the cold-flow phenomenon. This reference does not teach, describe or suggest the cold flow properties of the adhesive devices described in the present application. The Examiner stated in the Office action at page 3, second line from the bottom, that the physical strength of a polymer having a glass transition temperature below –50 degrees Celsius is not deteriorated by an increased extent of migration of drug and adjuvant (col. 2, lines 56-62). Applicant respectfully submits that the description "deterioration of physical strength by migration of drug and adjuvant" does not

correspond with the cold-flow problem described at page 5 of the specification of the present invention. Specifically, the reference does not teach or suggest a device having polymer structures whose glass transition temperatures decisively influence cold flow, such as those employed in the device of the present invention. As discussed in the specification, the layer(s) with the higher glass transition temperature(s) lead(s) to an improvement of the cohesion of the entire system. As a consequence, cold flow is reduced, so that the problem of the TTS's or DTS's becoming agglutinated with the primary packaging means during storage and leaving black edges on the application surface owing to residues of adhesive either no longer appears or is strongly reduced (page 9, lines 1-13, see also page12, lines 15-20). Therefore, one skilled in the art would not be motivated to refer to Otsuka in order to address the problem of cold-flow, nor would there be a reasonable expectation of successfully correcting the cold-flow problem.

Turning now to the Ercillo reference, the applicant submits that the reference does not concern active substance-containing adhesive devices. It is submitted that the present invention pertains to the field of pharmaceutical technology since it concerns active substance containing preparations. A person having ordinary skill in this field would not have considered active constructions such as those described by Ercillo which do not contain active substances. Ercillo concerns the field of adhesive label manufacture (col. 1, lines 32-45) and there is no indication therein that these labels were intended for medical use or that they may contain active substances.

Furthermore, Otsuka does not make any reference to non-medical adhesive compositions (col. 1, lines 20-44). The introductory part of the present specification does

not make any reference to non-pharmaceutical label technology. It is well known that the physical properties of adhesive layers may be severely affected by the presence of a pharmaceutical active substance. A person having ordinary skill in the art would not have considered a prior art document belonging to the field of non-medical adhesive labels.

Applicant submits that Ercillo attempted to improve the "convertibility" or to minimize the problems which occur when continuous rolls of adhesive tape are processed into individual labels by die cutting, matrix stripping, etc. It was found that this convertibility is improved when using a laminate of at least two adhesive layers. However, Ercillo, like Otsuka, does not address the problem of "cold flow." Therefore, the problem underlying Ercillo's invention is fundamentally different from the problem addressed by the present invention. Applicant therefore submits that because of this, one skilled in the art would not have considered this prior art when trying to improve the cold-flow properties of drug-containing adhesive systems.

As mentioned above, Otsuka does not teach or suggest an adhesive system having a third layer. The present invention as set forth in the claims as amended have a unique laminate structure comprising a central layer (or second layer) which is covered on both sides with a second/third layer and the polymers of these outer layers each have a glass transition temperature (T_g1 or T_g3) which is lower than the glass transition temperature (T_g2) of the central layer. One of the outer layers may serve as an adhesive layer while the respective other layer may be covered with a backing layer (claim 19). The layer having the higher glass transition temperature (i.e., the second layer) is responsible for improving the cohesion of the entire system (page 6, lines 10-12 of the present specification). This specific

construction is neither taught or disclosed in either Otsuka or Ercillo, alone or in combination.

Ercillo, like Otsuka, teaches the possibility of making a laminate comprising more than two layers. However, none of these prior art documents discuss the glass transition temperature of the additional layer or on the relative positioning of the third layer relative to the first two layers. Referring to Ercillo, the Examiner stated on page 4 of the Office action that if the glass transition temperature is too low, then the adhesive composition will flow readily. Accordingly, applicant submits that Ercillo in fact teaches away from the present invention since the claimed therapeutic systems comprise two (rather than just one) layers having a glass transition temperature which is lower than the glass transition temperature of the remaining layer (i.e., the central layer having T_g2). Following this teaching by Ercillo, applicant submits that one skilled in the art would not have considered adding a further layer having a glass transition temperature which is lower than that of the central layer, as it would have been expected that this would reduce the cohesiveness of the system.

Applicant further submits that it can be shown by the present invention that such a laminate does not exhibit cold flow over an extended period of time (present specification, Example on pages 7-8). An additional advantage of this layer arrangement is that this third layer can be formulated as an active substance-containing matrix layer (see Example 1, matrix layers 1a and 1b), thus increasing the total drug content (or dose).

Conclusion

For the foregoing reasons and amendments, it is believed that the present application as amended is in condition for allowance, and such action is earnestly solicited. The

Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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